



SUMMARY

Chapter 1 is a general introduction to this thesis. Acute respiratory tract infections (ARTI) are common clinical disorders, which can be caused by a wide range of viruses and bacteria. Outbreaks of respiratory infections, leading to substantial morbidity and mortality, may involve a major public health concern. For the implementation of appropriate control measures to limit further transmission, early detection of outbreaks is essential. In the Netherlands, continuous awareness for (sudden) shifts in the occurrence and characteristics of respiratory infectious diseases and pathogens is carried out by active surveillance, including the Dutch sentinel influenza surveillance system in a network of general practices and nursing homes. Unfortunately, the existing surveillance provides no data on the presence of respiratory pathogens in asymptomatic persons in the community. Moreover, the surveillance is limited to general practitioner (GP) consultations for influenza-like illnesses (ILI), while pneumonia is also a common respiratory disorder in the general population.

In this thesis we studied how the existing surveillance system can be enhanced, thereby supporting targeted control of respiratory infections in the Netherlands. Besides we evaluated the capabilities of the routine surveillance during the influenza pandemic in 2009.

AETIOLOGY

In the Netherlands, yearly about 900,000 persons visit their GP because of ARTI. A case-control study of ARTI in general practice patients, as described in **chapter 2**, confirmed that most ARTI have a viral cause. Rhinovirus was the most commonly detected pathogen in both patients consulting their GP because of airway complaints, and asymptomatic persons visiting their GP for complaints other than respiratory. These asymptomatic persons might be a neglected source of transmission.

The value of viral molecular diagnostics on sputum samples, used to establish the aetiology of community-acquired pneumonia in addition to conventional diagnostics, is described in **chapter 3**. Particularly in cases where diagnostics are essential to guide control measures, polymerase chain reaction (PCR) on sputum samples can be an important addition for both individual patient management and public health action.

EPIDEMIOLOGY

Chapter 4 showed that the detection of associations between environmental risk factors and respiratory infections is hindered by the heterogeneity in the general population as well as in pathogens causing ARTI. Exposure to persons with respiratory complaints was the only risk factor for respiratory infections found in a case-control study of ARTI in general practice patients. Since this exposure can hardly be avoided, increased awareness of the importance of hygienic measures is the most useful possibility to reduce the transmission of ARTI in the general population.

A population-based retrospective study on trends in pneumonia incidence in general practice, hospitalisation and mortality, as described in **chapter 5**, suggested that the morbidity of pneumonia in the Dutch population increased considerably in the period between 1997 and 2007. This increasing trend was most obvious in primary care. Most studies reporting pneumonia morbidity focused only on hospitalised patients, and might thereby have underestimated the increasing public health burden of pneumonia.

Chapter 6 discusses the labour-intensive design of the first few 100 cases and close contacts approach during the 2009 influenza pandemic, which resulted in a limited recruitment of cases as well as contacts. Nevertheless, the findings of the case-control study, aiming both to identify patient characteristics and risk factors for experiencing a symptomatic influenza A(H1N1)2009 infection in the general Dutch population and to get insight into the transmission of the influenza virus, were supplementary to those of case-based studies and important to guide control activities and for communication.

IMPACT

Chapter 7 presents a study relating the epidemiology of pandemic influenza in primary care ILI patients and in hospitalised patients with laboratory-confirmed influenza A(H1N1)2009 virus infection to the epidemiology of seasonal influenza. For this study we used a long-term validated sentinel GP surveillance system as well as a recently started nursing home network, both covering ILI activity and virological surveillance. This study showed that, while the absolute incidences of 2009 pandemic influenza were highest among children 0-4 years of age, the relative

clinical impact in the community compared to seasonal influenza in previous years was most noticeable in healthy children aged between 5 and 14 years of age.

Chapter 8 concerns a retrospective analysis of all notified deaths associated with a laboratory-confirmed influenza A(H1N1)2009 virus infection in the Netherlands both during the pandemic season 2009-2010 and the following influenza season 2010-2011. The mortality pattern in the influenza season 2010-2011 still resembled the pandemic season with a peak in relatively young age groups, but concurrently a clear shift toward seasonal patterns was seen, with a peak in mortality in the elderly, i.e. ≥ 75 years of age.

In **chapter 9** the findings of the earlier chapters are discussed and we considered how these can enhance the existing respiratory surveillance in the Netherlands. For many years, the sentinel ILI surveillance provides robust longitudinal data on ILI and influenza virus in the Dutch general practitioner population. Integrating pneumonia surveillance in the same population will strengthen this surveillance, and is important to understand the public health impact of both outbreaks and seasonal trends of respiratory infections. Furthermore, the 2009 influenza pandemic demonstrated the need for surveillance of severe acute respiratory infections (SARI) to assess and monitor the severity of outbreaks. Targeted well-designed case-control studies can supply additional information on key epidemiological, virological and clinical features needed for both control and communication, although they can be extremely challenging during outbreaks. During future pandemics, the pooling of epidemiological, virological and clinical data on both cases and controls of several countries should enable the collection of required data in a relatively short time period.